REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicants wish to reiterate their claim to the benefit of their Danish priority date of 16 May 2002 pursuant to the International Convention. Certified copies of Danish Patent Applications PA200200752 and PA200200753 have been made of record in PCT/EP03/05047 filed 14 May 2003 of which the instant application is the US National Phase. Acknowledgment of Applicant's perfected right of priority is respectfully requested.

Applicants have canceled claim 19 and amended claims 1 through 4, 18, 20, 21, 23, 26 and 27. Antecedent basis for the amendments to claims 1 through 4 and 23 may be found in the specification on pages 9 and 10 and in Example 1 which make it clear that the at least two foreign genes are homologous with respect to one another, and not with respect to the poxvirus. The amendments of claims 18 and 20 are purely of a formal nature and the amendment of claim 21 includes the word "isolated" before "cell" as requested by the Examiner to make it clear that transgenic animals are not being claimed. Claims 26 and 27 now presented have full antecedent basis for all terms appearing in the claim, wither in an earlier part of the claim or in claim 1 from which these two claims depend. The amendments to claims 26 and 27 now make it clear that it is the same DNA probe as claimed in claim 25 that is administered in claims 26 and 27 to either detect cells

infected with the new recombinant poxvirus according to the invention or to identify the recombinant poxvirus according to the invention in a biological sample. The use of the specific probe as covered in claim 25 to either detect cells infected with the new recombinant poxvirus or to identify the presence of a recombinant poxvirus in a sample according to the present invention using probes to effect hybridization is well known to those skilled in the art and is not beyond the scope of the enabling disclosure. Thus it is believed that all claims now presented are in full compliance with the requirements of both the first and second paragraphs of 35 USC 112.

The Examiner has rejected claim 12 under 35 USC 112, first paragraph, as based upon a non-enabling disclosure. The Examiner has indicated that the basis for the rejection is lack of adequate assurance that the viral vector MVA-BN has been permanently deposited in a depository and that access to the public will be given to the MVA-BN deposit once a patent issues in this application. The Examiner has specifically requested that someone with direct knowledge representing the Applicant sign a declaration stating that the deposit has been made in compliance with the requirements of MPEP 608.01(p)(C), Item 1. Applicants now enclose such a declaration signed by Dr. Petra Pielken, Applicants' patent attorney in Germany who has first hand knowledge that the deposits were made in accordance with the requirements of the Budapest Convention. Applicants also enclose an executed power of attorney executed by the assignee of the instant application, Bavarian-

Nordic in favor of Dr. Pielken. Submission of he declaration of Dr. Pielken is believed to overcome the rejection of claim 12 under 35 USC 112, first paragraph, as based upon a non-enabling disclosure.

Applicants also point out that MVA-BN is not a new poxvirus and that Bavarian-Nordic has already presented declarations in earlier filed US Patent Applications to establish that a deposit of MVA-BN has been made in a depository in full compliance with the requirements of the Budapest Convention. See Bavarian-Nordic's US Patents 6,913,752 and 6,761,893. Thus the rejection of claims 12 under 35 USC 112, first paragraph, has been obviated.

The Examiner has rejected claims 1 through 8, 10, 13 through 22, and 25 as anticipated in view of US Patent 5,744,141 to PAOLETTI et al. The Examiner has cited several passages throughout the PAOLETTI et al reference that she contends supports her contention that the reference anticipates the present claims. Applicants have looked over all of these passages, including Example 5 in cols. 9 through 12 of the PAOLETTI et al patent, and it does not appear that the reference discloses the insertion into a poxvirus of at least two homologous foreign genes in comparison to each other, wherein each of said genes is inserted into a <u>different insertion site</u> of the viral genome. PAOLETTI et al discloses the insertion of one or more foreign genes, which may be homologous to one another, at the same insertion site. For instance see Figures 1, 2 and 4 of PAOLETTI et al. The amendments to claims 1 through 4, and 23 now presented serve to even better

distinguish the present invention over the reference. It would not be obvious to one "skilled in the art" to insert two or more foreign genes, homologous to one another, at two different insertion sites in a poxviral vector to obtain a recombinant poxvirus. On structural grounds alone, Applicants do not believe that PAOLETTI et al would render the present recombinant poxviruses and the methods of using same, and the kits used to prepare same and test for same as obvious.

Furthermore Applicants have discovered that these recombinant poxviruses prepared according to the present invention are surprisingly stable immunogens and are not subject to homologous recombination as would have been expected. See page 9 of the application where it is mentioned that the foreign homologous genes, inserted at remote sites into the poxviral genome, would have been expected to be deleted. However, homologous recombination would not be expected to be a problem if the two foreign homologous genes abut one another as in PAOLETTI et al. It is noted that the frequency of recombination is proportional to the distance between the linked genes, and so events between two or more homologous genes located in different sites as in the present invention would be expected to be high, and conversely events between two abutting homologous genes in PAOLETTI et al would be expected to be low. See page 10 of the present application. Thus the fact that PAOLETTI et al discloses insertion of two homologous genes into the same site of a viral vector in no way is suggestive of the presently claimed invention.

The Examiner has also indicated that she believes that claims 9, 23 and 24 are obvious in view of PAOLETTI et al. Once again, Applicants' arguments set forth hereinabove to distinguish claims 1 through 8, 10, 13 through 22, and 25 over PAOLETTI et al should serve to patentably distinguish claims 23 and 24 over PAOLETTI et al as well.

The Examiner notes that Applicant's preferred poxviral vector is MVA-BN and that PAOLETTI et al uses vaccinia virus as a viral vector, but not MVA-BN. However, the Examiner has cited MEN et al to show that MVA-BN is a well known safe viral vector that is especially suitable as a vector because it is a highly attenuated virus and cannot replicate in mammalian cells. Accordingly the Examiner believes that the combination of PAOLETTI et al and MEN et al renders claims 11 and 13 obvious as well. Once again, the arguments that Applicants have set forth hereinabove to distinguish the claims over PAOLETTI et al, also patentably distinguish claims 11 and 13 over the combination of MEN et al with PAOLETTI et al.

Applicants now have the following direct comments regarding the patentability of the presently claimed invention over the cited prior art:

Turning to the cited US Patent 5,744,141 please note that the content of said patent corresponds to US Patent 5,514,375 which is cited and discussed in the specification on page 10, lines 17 to 26. All comments on US Patent 5,514,375 as given in the specification do fully apply to US Patent 5,744,141 cited by the Examiner. Accordingly, also US Patent 5,744,141 discloses

insertion of flavivirus genes into the same insertion site. Additionally the flavivirus genes inserted into the poxviral genome according to US Patent 5,744,141 only show a homology of 20.2 to 29.6%, i.e. the genes according to the disclosure in the patent cannot be considered as being homologous to each other, but are clearly heterologous. See also the definition given in the present specification on page 11, last paragraph (i.e. homology of at least 50%). Thus recombination events after insertion of genes with such a low homology would not have been expected. It is expected rather by one skilled in the art that such heterologous genes with respect to one another would be stably inserted into the genome.
Even if the genes in the recombinants disclosed in US Patents 5,514,375 and 5,744,141, respectively, would reveal a higher homology, it would be much more unlikely that recombination events occur, because the genes are inserted into the same insertion site. As explained in the specification on page 10, first paragraph, the frequency of recombination is proportional to the distance between two linked genes, i.e. when two homologous genes abut one another or are inserted right next to each other in the genome, the frequency of recombination is very low and recombination events are, thus, very unlikely. And even if in such a case recombination between homologous genes would occur, it is further also unlikely that genes of the virus itself which may be involved in the viral life cycle and in amplification of the virus, respectively, are lost, because there are surely no viral genes included in the space between the inserted homologous genes when both homologous genes

abut one another or are inserted right next to each other in the same insertion site of the genome.

Applicants are enclosing a copy of A FUNCTIONAL MEASLES VIRUS REPLICATION AND TRANSCRIPTION..." , Paul M. Howley et al, XP-002257129, Journal of Virological Methods 79 (1999) pp 65 to 74. The reference was made of record along with Form PTO 1449 at the time that the application was filed in the United States. However, Applicants note that the Examiner has not initialed this reference on the Form PTO 1449 attached to the back of the office action, indicating to Applicants that the reference may have been lost. Therefore Applicants are now providing another copy of the reference on a new Form PTO 1449.

Favorable action in this case is earnestly solicited.

Respectfully submitted,
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Enclosures: PTO 1449 and Reference (1)
Declaration of Deposit of Microorganism
Power of Attorney